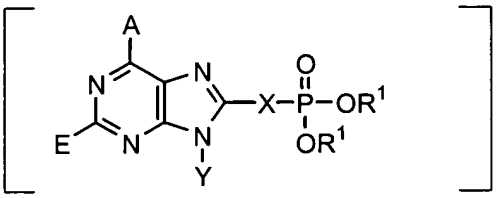
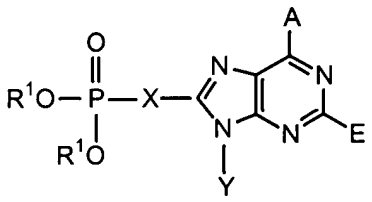
IN THE CLAIMS

Claims 2-33, 40 and 43 were cancelled without prejudice.

Claims 1, 34-37, 39, and 42 were amended as follows with the noted changes:

1. (Amended) A compound of formula 1:





wherein

A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

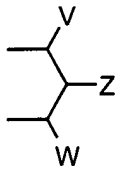
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl,

[alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

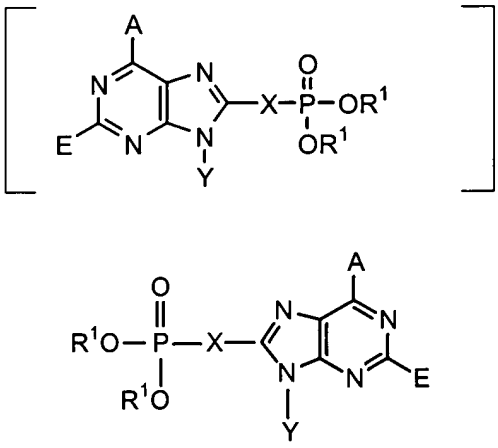
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

34. (Amended) A method of treating an animal for diabetes mellitus, comprising administering to said animal a therapeutically effective amount of a compound of formula (1):



wherein

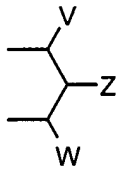
A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2{}_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2{}_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy,

alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

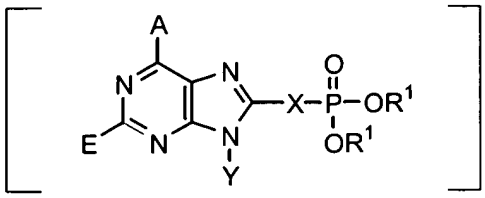
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

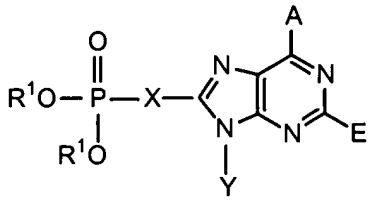
$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

35. (Amended) A method of lowering blood glucose levels in an animal in need thereof, comprising administering to said animal a pharmaceutically acceptable amount of a compound of formula (1):





wherein

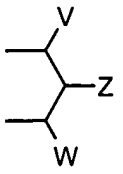
A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -$R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -$CH_2OH$, -$CH_2OCOR^3$, -$CH_2OC(O)SR^3$, -$CH_2OCO_2R^3$, -$SR^3$, -$S(O)R^3$, -$CH_2N_3$, -$CH_2NR^2_2$, -$CH_2Ar$, -CH(Ar)OH, -$CH(CH=CR^2R^2)OH$, -$CH(C\equiv CR^2)OH$, and -$R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is -$R^2$, then at least one of V and W is not -H or -$R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -$C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)$R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

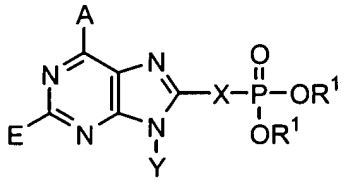
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

$R^{10}$ is selected from the group consisting of -H, lower alkyl, -$NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, -$NH_2$ and -$OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

36. A method of inhibiting FBPase at the AMP site in patients in need thereof, comprising administering to said patients an FBPase inhibitory amount of a compound of formula (1):



wherein

A is selected from the group consisting of -$NR^8_2$, -$NHSO_2R^3$, -$OR^5$, -$SR^5$, [halogen] halo, lower alkyl, -$CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

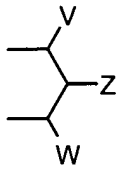
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -$NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)$R^3$, -$S(O)_2R^3$, -C(O)-$OR^3$, -$CONHR^3$, -$NR^2_2$, and -$OR^3$,

all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, -CH(Ar)OH, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

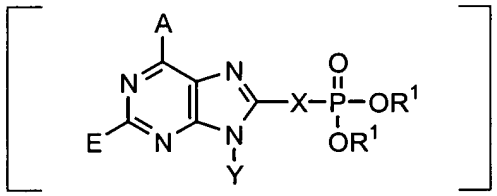
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

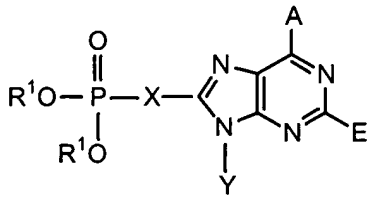
$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

37. (Amended) A method of inhibiting gluconeogenesis in animal in need thereof, comprising administering to said animal an effective amount of a compound of formula (1):





wherein

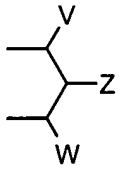
A is selected from the group consisting of -$NR^8_2$, -$NHSO_2R^3$, -$OR^5$, -$SR^5$, [halogen] halo, lower alkyl, -$CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -$NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -$C(O)R^3$, -$S(O)_2R^3$, -C(O)-$OR^3$, -$CONHR^3$, -$NR^2_2$, and -$OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -$C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, -$C(R^2)_2OC(O)NR^2_2$, -$NR^2$-C(O)-$R^3$, -$C(R^2)_2$-OC (O)$R^3$, -$C(R^2)_2$-O-$C(O)OR^3$, -$C(R^2)_2OC(O)SR^3$, [alkyl-S-$C(O)R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -$R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy,

acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

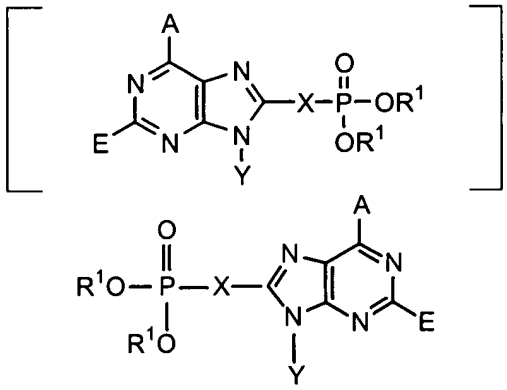
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

39. (Amended) A method of treating an animal for a disease derived from abnormally elevated insulin levels, comprising administering to said animal a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor wherein said inhibitor is a compound of formula (1):



wherein

A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

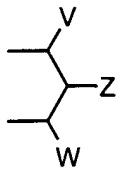
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and

$R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2{}_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH{=}CR^2R^2)OH$, $-CH(C{\equiv}CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

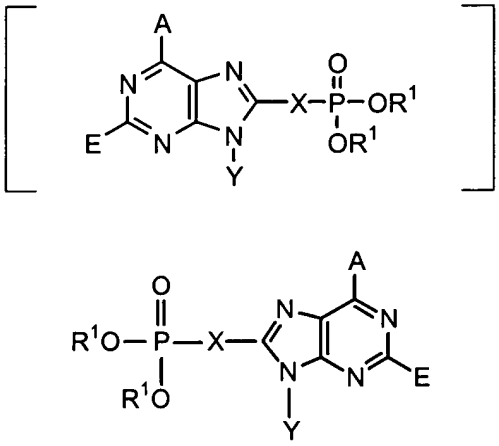
$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

42. (Amended) A method of treating an animal with excess glycogen storage disease, comprising administering to said animal in need thereof a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor, wherein said inhibitor is a compound of formula (1):



wherein

A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

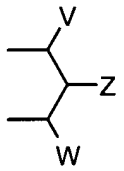
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl,

aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

$R^1$ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, [alkylaryl] –alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)$R^3$] –alk-S-C(O)$R^3$, [alkyl-S-S-alkylhydroxy] –alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] –alk-S-S-S-alkylhydroxy, or together $R^1$ and $R^1$ are [-alkyl-S-S-alkyl-] –alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together $R^1$ and $R^1$ are




wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$R^5$ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$R^6$ is independently selected from the group consisting of -H, and lower alkyl;

$R^7$ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

$R^8$ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said $R^8$ groups form a bidendate [alkyl] alkylene;

$R^9$ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

$R^{10}$ is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

$R^{11}$ is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.